



# Continuous regulation of liquids

Customised valve and sensor solutions for any control loop

We make ideas flow.

**bürkert**  
FLUID CONTROL SYSTEMS



# Customised valve and sensor solutions for any control loop

In order to efficiently manufacture high-quality pharmaceutical and biotech products, it is of great importance to have continuous fluid process control with precise modulation capabilities. If the control loops work, maximum quality can be generated with minimum consumption of resources. The focus is on your individual requirements. The selection, dimensioning and coordination of the required components are different for each control loop. At Bürkert, we not only

have decades of planning experience, but we also have the right automation solutions to offer you. With our portfolio of valves, actuators and sensors we offer tailor-made solutions for continuous liquid control. The products are not only available individually but also as coordinated modular systems consisting of control loops, sensors and accessories. We would be happy to advise you personally on this.

## Constantly safe, operating cost-optimised closed-loop control of WFI systems

Water for Injection (WFI) systems in the pharmaceutical industry require special treatment. Quality needs to be controlled and documented and flow rates need to be measured and regulated so that purity and availability can be consistently guaranteed. The amounts of energy required to produce, distribute and store WFI result in significant operating costs. At the same time, environmental protection and sustainability are becoming increasingly important at many pharmaceutical companies. This makes the energy efficiency of a plant an important issue in the overall investment decision.

## Continuous, precisely regulated nutrient supply for bioreactors

A bioreactor's purpose is to provide the most effective possible product yield. This requires precise control of all parameters in order to best support the fermentation process. The type and concentration, the temperature, oxygen content and pH value of the nutrients are critical. Reproducible processes are fundamental to consistently high product quality. Find out which technologies, solutions and consulting services you can use to optimise your fermenters and reduce machine costs.



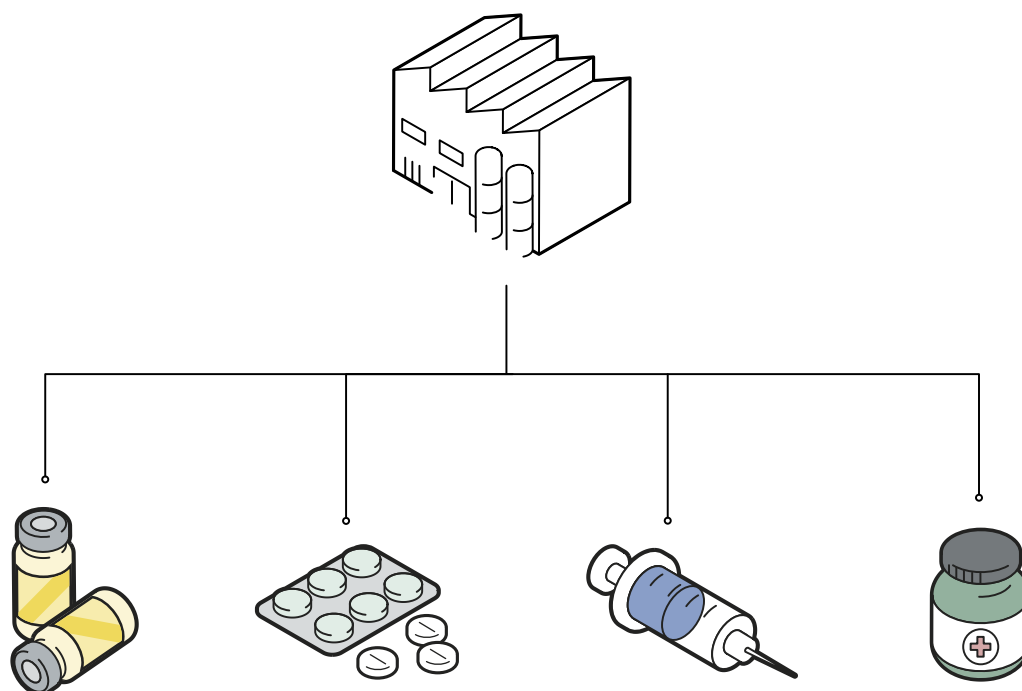


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# WFI – a valuable raw material

In the pharmaceutical industry, generating a consistently sufficient supply of water for injection purposes (WFI) is an important secondary process. Due to elaborate manufacturing processes, WFI is a valuable raw material that is often required in large quantities and is therefore often produced from drinking water directly on site. The purity of

the water has clearly defined limit values for microbiological loads in the form of colonizing units, conductivity and amount of organic carbon. The constant regulation and distribution of WFI is a decisive factor in making your pharmaceutical production processes safe, reliably and compliant with quality standards.



# WFI system for pharmaceutical production

On the one hand, WFI is transferred from a WFI circuit to the system to clean the pipelines, and on the other hand it is used as part of the recipe in a variety of drugs. In order to ensure the water quality and availability for the production process at all times, numerous measurement parameters must be collected via sensors in the WFI loop and compared with the set-point values. In addition, it is important

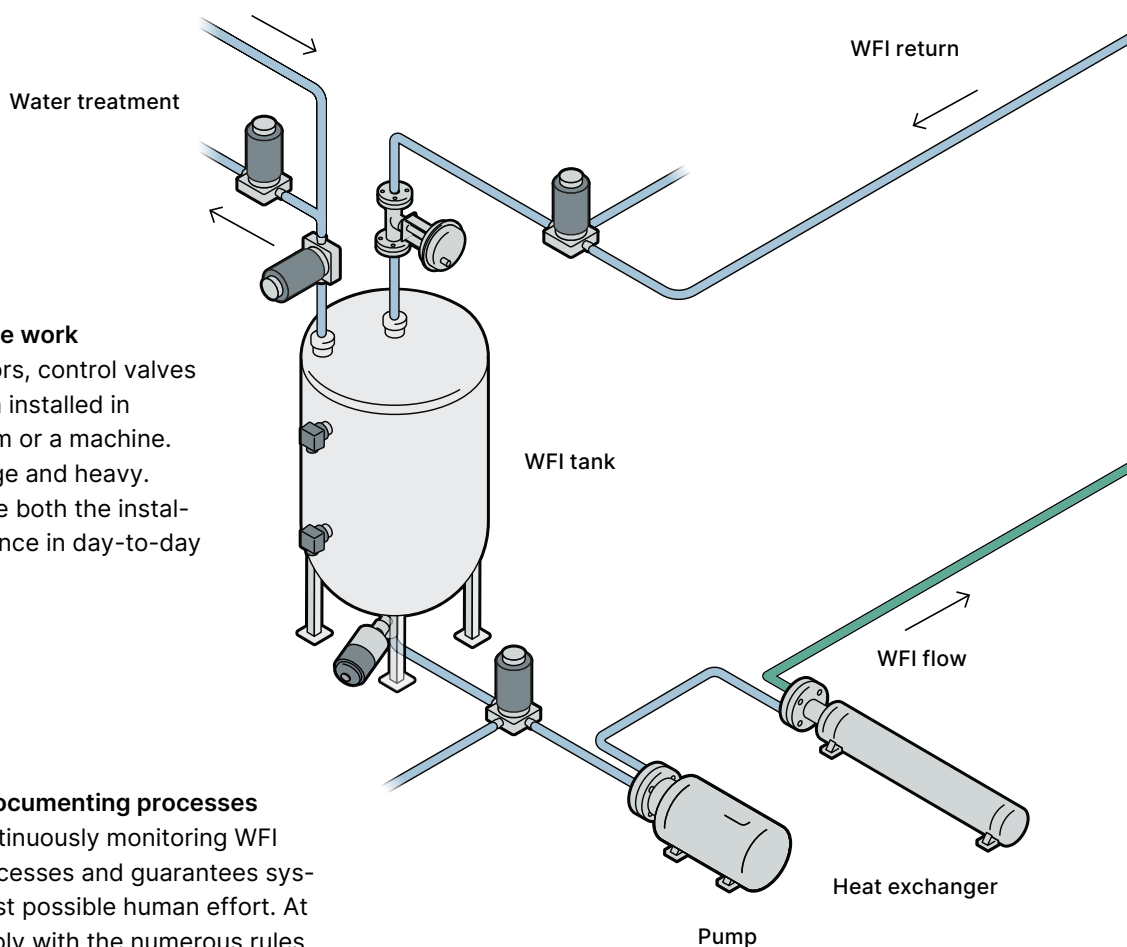
to regulate and precisely control the extraction of the water and to document it in a verifiable manner. Since WFI is a significant cost factor in the manufacture of medical products, it must be used sparingly for both economic and ecological reasons. There are numerous challenges to be overcome in these ongoing processes.

## Avoiding extensive maintenance work

Flow meters, temperature sensors, control valves and other components are often installed in hard-to-reach places in a system or a machine. The devices are also usually large and heavy. These factors usually complicate both the installation and subsequent maintenance in day-to-day production.

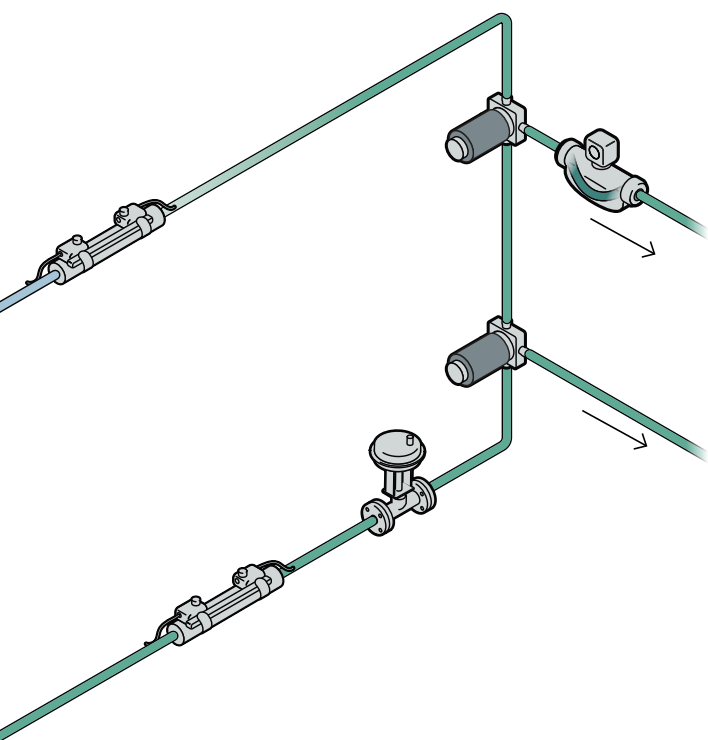
## Continuously monitoring and documenting processes

There are many reasons for continuously monitoring WFI loops. It secures production processes and guarantees system availability – all with the least possible human effort. At the same time, it serves to comply with the numerous rules and regulations in the pharmaceutical industry, which require complete documentation of the measurement parameters to produce clear traceability.



### Reliably measuring and recording WFI consumption

The costs of processing WFI and storing it add significantly to overall operating costs. As such, daily WFI consumption is measured as precisely as possible. In addition, conclusions can be drawn about possible errors or defects in certain process steps, for example if the daily consumption is unusually high. Measuring flow rates is often done with the help of ultrasonic clamp-on sensors, but they are prone to errors and comparatively imprecise so determining exact daily quantities is difficult with them.



### Precisely regulating the amount of liquid at tapping points

If too much WFI is taken out of the loop it results in unnecessary additional costs. WFI is a significant cost factor in the manufacture of medical products and must be used sparingly for both economic and ecological reasons. Diaphragm valves can be used to regulate WFI extraction because they comply with the demanding legal hygiene standards in the pharmaceutical industry. The problem is that they are rather imprecise. To compensate for this, expensive and heavy control actuators are often designed specifically for this task.

### Checking flow rates of WFI quantities at point of use

To control WFI flow rates at point of use, conventional structures often use Coriolis measuring devices, but these are usually expensive to purchase and operate. Because they reduce pipelines, they also increase pumping costs. In addition, their size and weight make them cumbersome to install. Yet alternatives are hard to find: Magnetic inductive flow meters do not work due to the low conductivity of WFI while mechanical measuring techniques don't meet the hygiene requirements of the pharmaceutical industry.

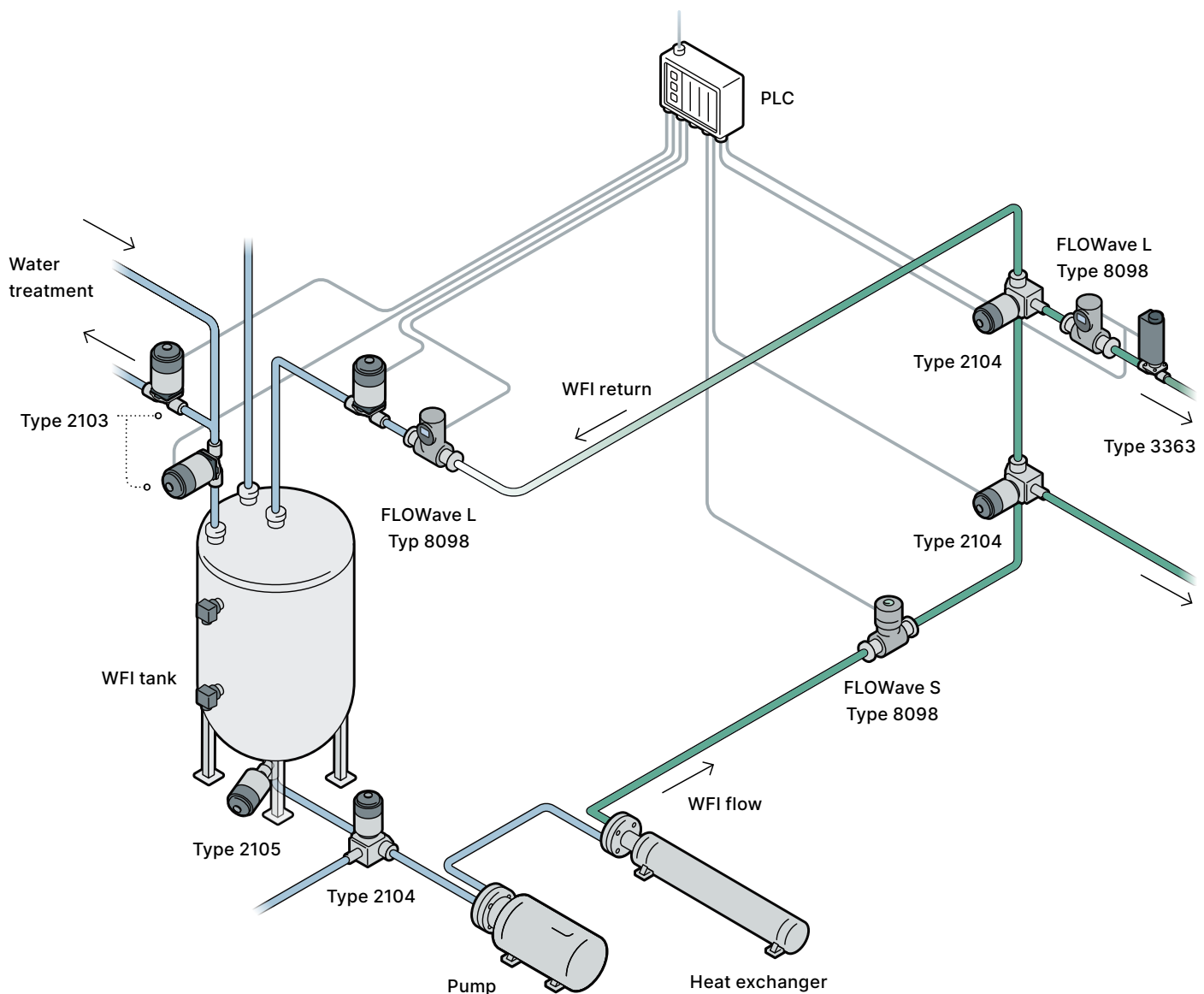
### Preventing contamination from biofilm

The speed and temperature in a WFI loop should always correspond to the industry guidelines so that no harmful biofilms can settle in the pipelines. It would contaminate the WFI and thus the pharmaceutical products. Volume flow and temperature are therefore measured with a flow rate and temperature sensor, then monitored and permanently documented to comply with legal regulations. Ultrasonic clamp-on sensors are often used in conventional applications. Calibrating them is time consuming. The solution is also susceptible to electromagnetic influences, which in turn often makes measurement results less accurate.

# Customised systems for regulating and controlling WFI loops

The quality and constant availability of your ultrapure water is a decisive factor in the quality of your products. The manufacture, storage and transport of WFI for the pharmaceutical industry is complex and needs to withstand continuous controls. Bürkert can help you to keep an eye

on, regulate and document the water quality and availability of your WFI loop, around the clock in a time-saving manner. This way you can react quickly to deviations and avoid process failures or faulty batches.





### Optimised control systems reduce WFI consumption

Bürkert control solutions are designed to exactly match each customer's requirements. A local control loop for extracting ultrapure water from the WFI circuit in production processes ensures extremely precise water dosing, for example in conjunction with individually designed components. The result: Overdosing is a thing of the past and system efficiency increases. Another advantage of the Bürkert solution is quick response times. Our valves can switch immediately in the event of an undesired process deviation and prevent contamination or incorrect dosing. Another potential for time savings lies in the procurement of spare parts: both custom components and prefabricated systems can be ordered quickly from Bürkert suppliers at any time.



### Correct valve design ensures high process efficiency

When manufacturing pharmaceutical products, it is not just hygienic stainless steel components with small dead spaces that are required. The ability to exactly regulate WFI cycles and document the corresponding parameters is also a must. However, extraction processes from the WFI loop can only be precisely controlled if the control valves are designed appropriately. Correct dimensioning means optimal use of a valve's stroke range, which ensures sufficient flow reserves. Bürkert helps you configure the right valve for your application in order to increase process reliability and avoid unnecessary additional costs for components and operating costs.



### Electromechanical drives enable high-precision control without compressed air

For applications that require highly precise control and where compressed air is not available or is undesirable, valves driven by electric motors offer a perfect solution. The electromotive version enables higher resolution so that regulation is even more precise than with pneumatically operated valves. Since the electric actuator allows almost stepless valve operation, the amount of WFI flowing through the valve can be very carefully controlled. „Overshooting“ can be avoided this way when operating the control valve.



### Flow rate and temperature measurements ensure constant product quality

Bürkert engineers developed FLOWave to help you carry out hygienic, high-precision flow rate measurements. Thanks to our innovative SAW technology, volume flow and temperature can be determined without any sensor elements in the measuring tube – regardless of the conductivity of the media. This is confirmed by various certificates (ASME BPE, 3A and EHEDG). The new measurement method in the pipe is not only very precise but also facilitates integration into the WFI loop. Their greatest advantage is that it reduces the risk of contamination: where there is no dead space, there is no contamination. The smooth FLOWave surface is tapered at the measuring point, complies with the stringent hygiene requirements of the pharmaceutical industry, prevents deposits and pressure drops, and ensures germ-free cleaning. This guarantees the safety of the active pharmaceutical ingredients at all times.



### Solenoid valve technology reduces energy consumption

Electricity is required to generate compressed air – a major cost factor in the operation of pharmaceutical water systems. Conventional valve technology requires a constant supply of compressed air in order to regulate the steam supply through the process valve and thus ensure precise control of the WFI in pharmaceutical production. By contrast, Bürkert uses solenoid valve technology, which only consumes compressed air when the valve position needs to change. This reduces energy consumption and therefore operating costs.

# Targeted consultation for customised control loops

We would like to take the pressure off of you and help you find your ideal solution. That is why Bürkert supports you from the individual design of the control loop to the selection and dimensioning of the valves required in the process – including actuator technologies – all the way through to the appropriate automation solution. This way you not only

accelerate processes but also increase system efficiency and save planning, start-up and operating costs. We personally select and, if necessary, pre-assemble all the required components (valves, actuator technology, pipelines) in consultation with you.

## Solution



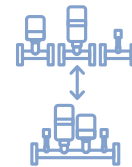
Analysis



Consultation



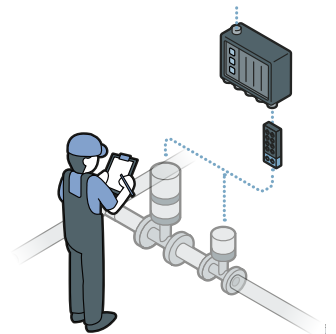
Interpretation



Components /  
systems



Start-up



# Example calculation

### Preventing additional costs incurred by imprecise regulation:

Thousands of cubic metres of WFI are required every year in pharmaceutical production facilities. Groundwater has to be processed in a complex distillation plant in order to be suitable for use as WFI. If you compare the price of classic tap water with WFI you will see that WFI costs almost three times as much. Even if WFI is treated using a membrane

system, the price is almost twice as high as that for the same amount of drinking water. In our calculation example, we assume that a pharmaceutical production site requires a Cv value of 40 (DN 40) for the WFI loop or the extraction points, and that the price for a cubic metre of WFI is €5. The following shows how much WFI – and money – is wasted due to imprecise regulation.

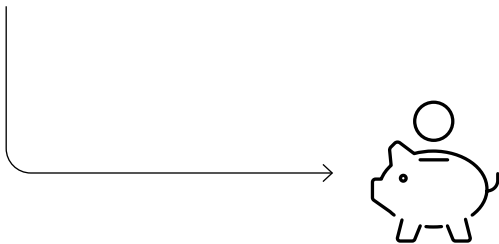
Additional consumption due to inaccurate regulation: **2 m<sup>3</sup>/h**

Production time per day: **8 hours**

Unwanted additional consumption in the 8 hours of: **approx. 16 m<sup>3</sup>** (2 m<sup>3</sup> x 8 h)

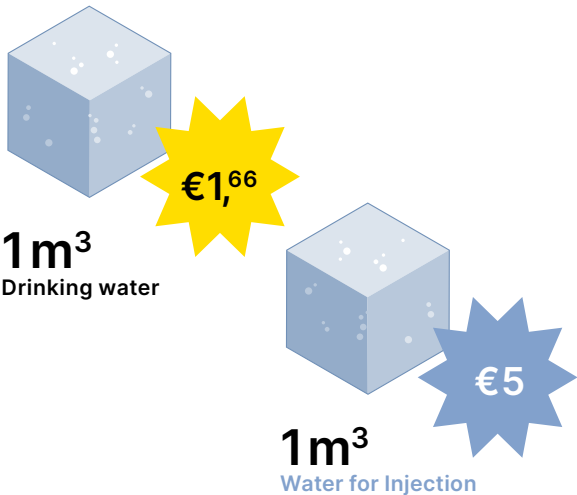
Additional costs per day due to additional consumption: approx. **€ 80** (16 m<sup>3</sup> x € 5)

Additional costs due to additional consumption, per year (230 working days):



**€ 18.400**

The additional costs in this calculation example can be saved with an precise control unit.



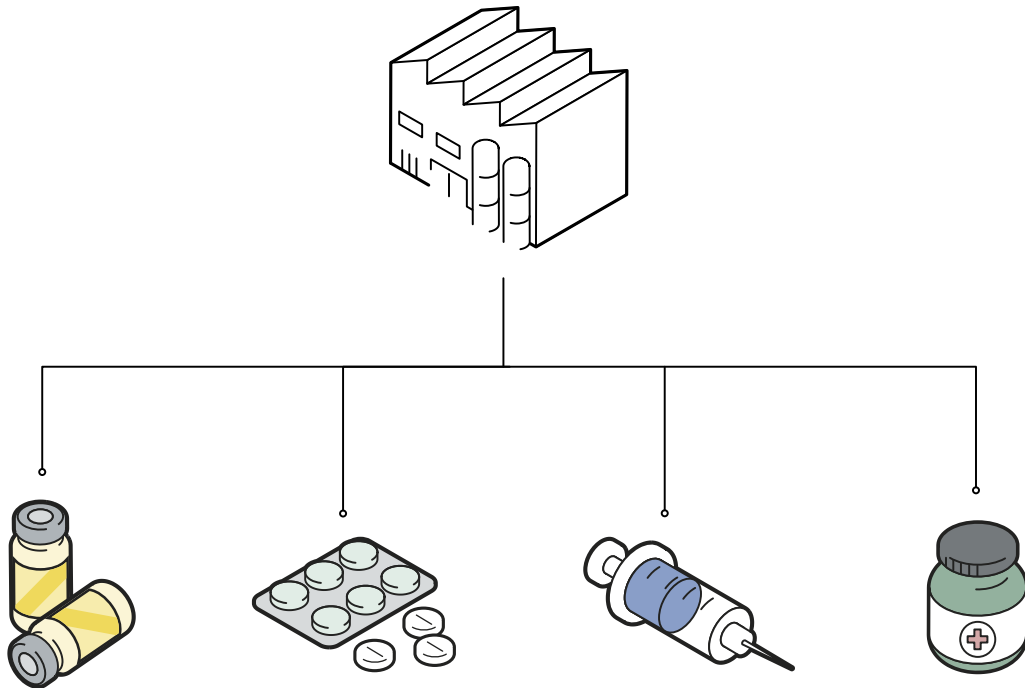


# Continuous, precisely regulated nutrient supply for bioreactors

## Create reliably reproducible processes

Continuous fermentation processes are often used in the manufacture of pharmaceutical products. In order for fermentation processes to run as economically as possible, all of the appropriate bioreactor parameters must be

continuously checked and regulated. When developing a fermentation unit, it is therefore crucial to create reliably reproducible processes. Additional requirements for modern machines include minimal effort during start-up and a flexible, compact system design.



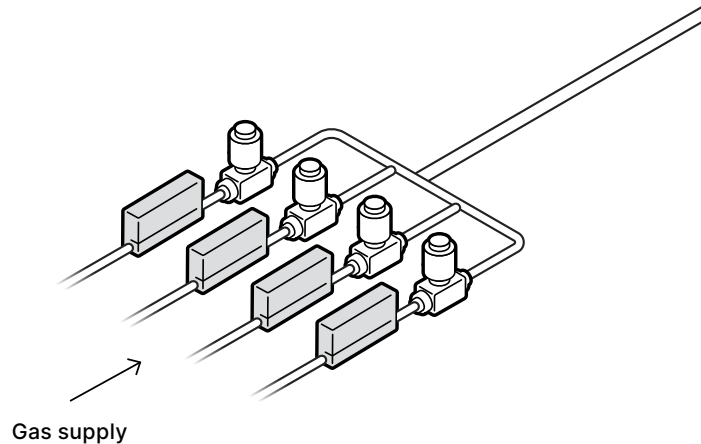
# Precise control as a vital factor in the success of fermentation processes

Bioreactors are continuously fed with nutrients while the fermentation process is running, while the end product is continuously and simultaneously removed. In order to precisely determine the required nutrient quantities, the variable to be regulated needs to be permanently calculated based on oxygen consumption of the microorganisms and then compared with a target value. To do this, the output

variable is measured with a corresponding sensor and fed back. The characteristic of closed-loop control is a closed control loop. The constant regulation is used to continuously adjust certain variables to specified target values and avoid disturbances. The design of the control loop determines the quality of the closed-loop control – accuracy, speed and stability must be exactly right.

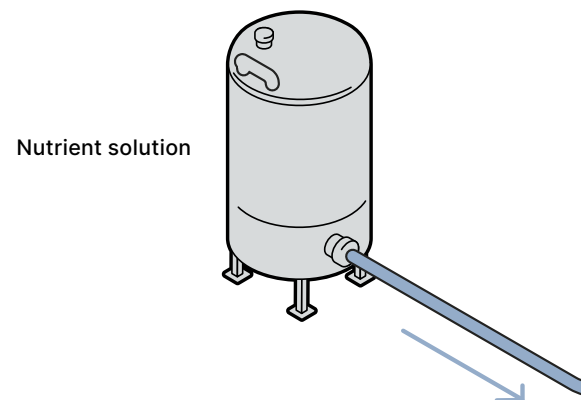
## Continuously monitoring and documenting processes

There are many reasons for continuously monitoring correct nutrient supplies to bioreactors. The procedure is intended to secure production processes and guarantee system availability – all with the least possible human effort. At the same time, it serves to comply with the numerous rules and regulations in the pharmaceutical industry, which require complete documentation of the measurement parameters to produce clear traceability. Good process controls should meet as many of these requirements as possible.



## Optimising complexity and installation

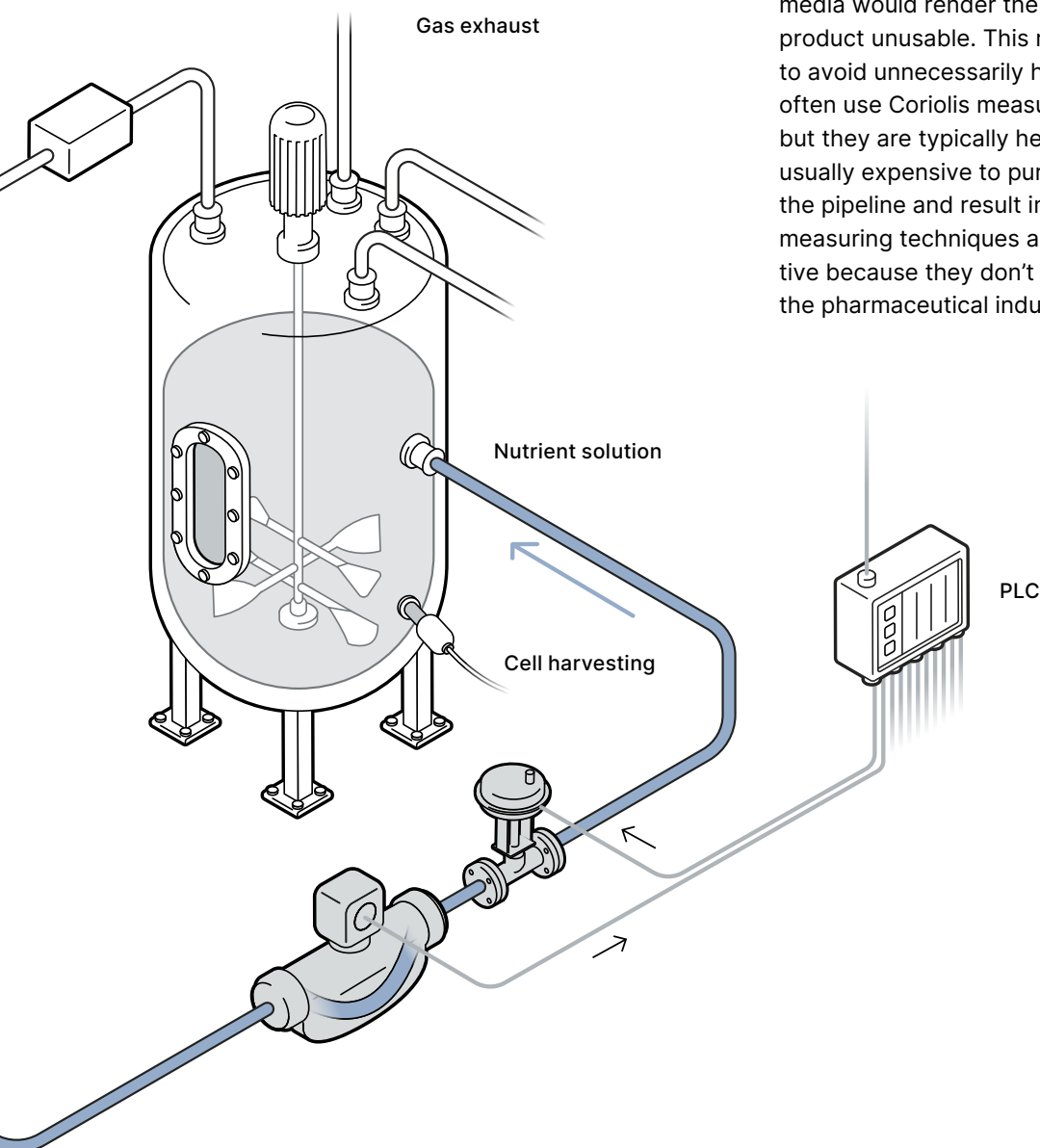
Flow meters, temperature sensors, control valves and other components are often installed in hard-to-reach places in a system or machine. In addition, the devices are usually large and heavy – a conventional flow meter and a similar valve combined can easily weigh 18 to 20 kilograms. These factors make both installation and subsequent maintenance in everyday production more difficult. In addition, all components must be optimally designed, coordinated and networked according to the target specifications of the fermentation process. This takes a lot of time, both for the development of the control loop and for the logistics and installation of the system.



### Preventing incorrect dosing and ensuring process reliability

Fresh nutrient solution is continuously fed to the culture system in the bioreactor – at an equally continuous flow rate. But it is actually not always the same. It needs to be regulated in terms of quantity according to the specifications in the various phases of fermentation. Since biochemical processes react extremely sensitively to changed parameters, neither too little nor too much solution can be added. If the specified process is disturbed, this has negative effects on cell growth and means that all of the substances added up to this point become unusable.

The result: unnecessary costs and sometimes considerable delays. Diaphragm valves are often used to regulate the supply of nutrient solution. Despite meeting the demanding legal hygiene standards of the pharmaceutical industry, however, they do not have optimal control characteristics. To compensate for the lack of accuracy, expensive and heavy control actuators often come into play that have to be specially designed for this task.



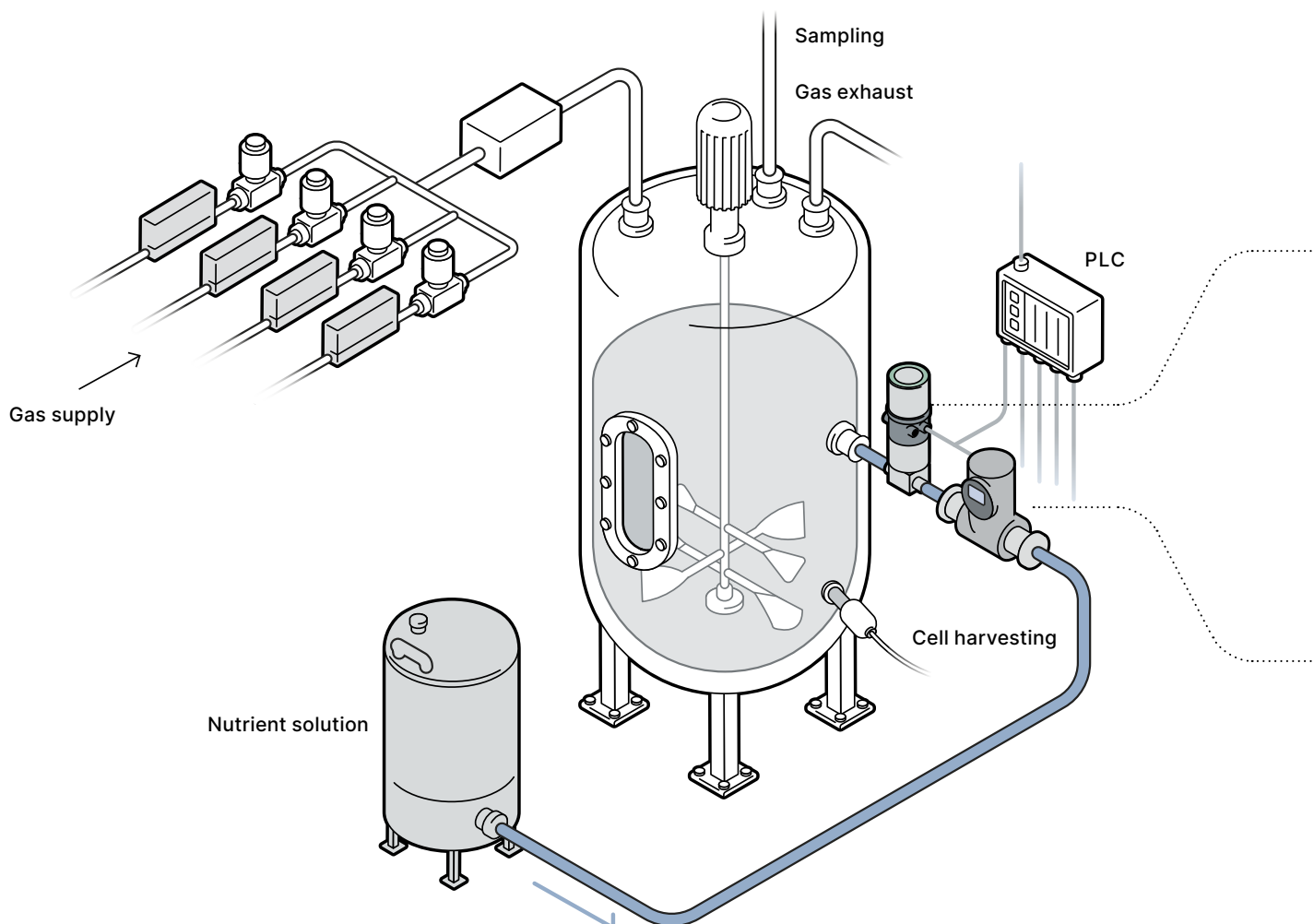
### Excluding contamination

For fermentation to function reliably, it is important that production and purification cycles are safely separated from each other. Contamination by foreign germs or CIP media would render the entire batch of the fermented product unusable. This results in lost time and money. In order to avoid unnecessarily high costs, conventional systems often use Coriolis measuring devices to control flow rates, but they are typically heavy and unwieldy. They are also usually expensive to purchase and operate. They reduce the pipeline and result in higher pumping costs. Mechanical measuring techniques are out of the question as an alternative because they don't meet the hygiene requirements of the pharmaceutical industry.

# Safely, quickly and automatically controlling the continuous supply of nutrients into bioreactors

Your machines can only ensure efficient production processes and high-quality end products if all of the control loops are functioning properly. Valve dimensioning and control loop design are often complex and time-consuming. That's why we do it for you. For example, we ensure that a local control loop for feeding nutrient solutions is combined

with individually designed components to ensure precise dosing and that adapts to the variable requirements in the fermentation process at any time. Since the control loop is constantly monitored, overdosing becomes a thing of the past and overall system efficiency increases.



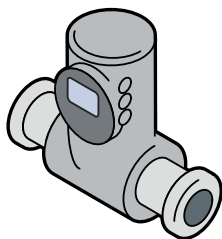


### Achieving fast response times with coordinated components

Unlike conventional solutions, the Bürkert solution provides a local control loop that ensures the direct exchange of information between the flow meter and the bellows valve. In this example application, the bellows valve regulates the amount of nutrient solution to be added based on information from FLOWave. The connected PLC not only monitors the process, but also compares the quantities supplied via the local control loop with the actual requirements of the fermenter, which are calculated from numerous measured values. Since the two components are constantly exchanging information, the reaction times for adjusting the amount of liquid are extremely short. If you need support with the correct design of the control loop, with the selection of suitable automation solutions or with the start-up and configuration of FLOWave, Bürkert's experts will be happy to assist you.



Bellows valve including  
ELEMENT positioner



FLOWave Type 8098



### Making flexible, compact systems a reality

Compared to conventional solutions, compact Bürkert components can create significantly more space-saving and flexible machine concepts. And not only that: In order to prepare for the challenges of the present and the future, Bürkert integrates modern digital connectivity into all of its positioner controllers, for example to high-level field buses or an IO-Link. This way the components can be seamlessly integrated into your control systems, which minimises the complexity of the system in many ways: during engineering, installation, integration and start-up as well as during operation and maintenance.



### Reducing complexity in development and procurement

Almost independently of the application in question we can offer you control solutions for fluidic processes that are tailored to your specific requirements, for example in fermentation processes. They can be either as perfectly selected and dimensioned products or as complete control loops that reduce customer effort in engineering and manufacturing processes. System solutions can typically reduce overall costs compared with purchasing individual components. In the planning stage we take the valve dimensioning and control loop design process off your hands. This saves you time and money.



### Minimising installation and start-up costs

Control loop start-up is often tedious and time-consuming. But there are ways to speed up the process: Bürkert simplifies start-up with an autotune function that is included as a standard feature of most positioners. It ensures that the controller automatically adapts at the push of a button to the system conditions. In addition, the lower weight and more compact designs of Bürkert's solutions contribute to quick installation – even in hard-to-reach places or high installation locations.

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## Solution



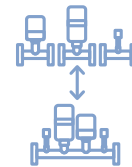
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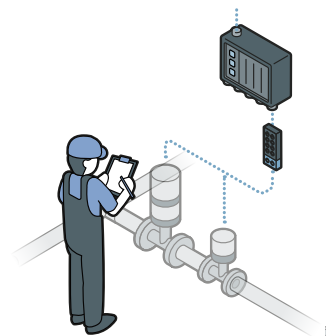
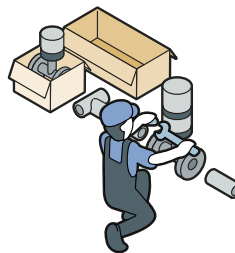
Interpretation



Components /  
systems



Start-up



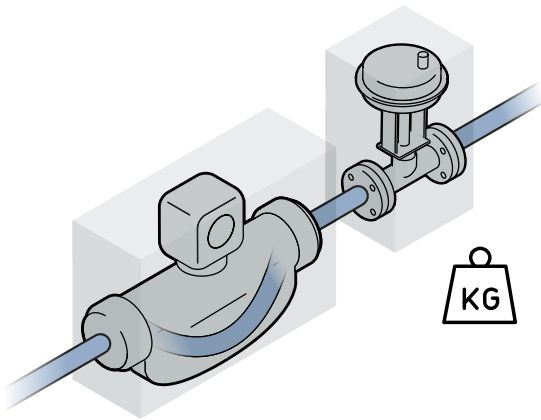
# Example calculation

## Saving space and weight:

In conventional solutions, the total weight of the two components required for controlling nutrient solution feeds into bioreactors is around 18.5 kg, assuming a DN of 1/2" each. By contrast, the total weight of the Bürkert solutions with the same DN is only 4.4 kg. In addition to the significant

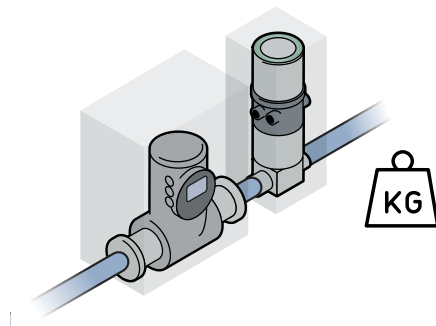
weight savings of more than 14 kg, the Bürkert version requires significantly less space, which leads to more flexible system concepts, shorter installation times and lower machine costs.

Conventional solution



Conventional flow meter (DN 1/2")	6.5 kg
Conventional valve (DN 1/2")	12.0 kg
<b>Total weight of the two components</b>	<b>18.5 kg</b>

Bürkert solution



FLOWave (DN 1/2")	3.0 kg
Bürkert valve (DN 1/2")	1.4 kg
<b>Total weight of the two components:</b>	<b>4.4 kg</b>

**14.1 kg**

Lighter with Bürkert solution

**Bürkert Fluid Control Systems**  
Christian-Bürkert-Straße 13-17  
74653 Ingelfingen  
Germany

Phone: +49 7940 100  
info@burkert.com

[www.burkert.com](http://www.burkert.com)

**bürkert**  
FLUID CONTROL SYSTEMS